Remarks/Arguments:

Status of Claims

Claims 1, 11 and 14-27 are in the application.

By way of this amendment, claims 1, 16 and 22 have been amended.

Upon entry of this amendment, claims 1, 11 and 14-27 will be pending.

Summary of the Amendment

The claims have been amended to place them in allowable form or otherwise place them in better condition for appeal.

Claim 1 has been amended to more clearly refer to the quantitative measurement set forth in the claim. As the claim clearly states, it relates to "[a] method for quantifying molecules expressing a selected epitope in a sample..." The final step of the claim has been amended to add reference to the measurement of fluorescence to quantify the molecules present. Support for the amendment is found specifically on page 3, lines 26-28 of the specification.

Claims 16 and 22 have been amended to be presented as independent claims, incorporating all of the limitations of the claims from which they previously depended.

No new matter has been added. No new issues of patentability have been raised.

Double Patenting Rejections

Claims 1, 11, 13 and 14 remain provisionally rejected under the judicially created doctrine of obvious-type double patenting over claims in co-pending applications 09/624,946 and 09/977,716. Applicants note that this rejection is provisional. Applicants will promptly provide a terminally disclaimer if appropriate and as necessary upon indication of allowability of claims in the instant case.

Premature Final Rejection

Applicants respectfully urge that the rejection of the claims has been made final prematurely. Applicants respectfully urge that the Official Action contains a new ground of rejection not necessitated by an amendment made by Applicants or Information disclosure statement

filed during the period set forth in 37 C.F.R. 1.97(e) with payment of a fee. Accordingly, the new ground of rejection renders the making of the rejection final premature.

Specifically, while claims 1 continues to be rejected under 35 USC §103 in view of Eberwine and Sano as discussed below, the new Official Action argues that the claim does not recite that the method claim contains a limitation that is quantitative. (See page 2 of the Official Action dated February 12, 2004.) This point was not raised in the earlier Official Action which states that one skilled in the art would be motivated to combine the teachings of Eberwine and Sano "in order to quantify molecules expressing a selected epitope in a sample." (See page 6 of the Official Action dated May 30, 2003.) Accordingly, for the first time, the Office is asserting in the Official Action dated February 12, 2004 that the claim lacks a limitation directed to quantification needed to distinguish over the combination of Eberwine and Sano. Thus, the final rejection is premature.

In the event that Applicants amendment of claim 1 does not place the claim in allowable form, Applicants respectfully requests that the finality of the rejection be withdrawn.

Rejections under 35 USC §103

Claim 1 rejected in view of Eberwine and Sano

Claim 1 is rejected under 35 USC §103 in view of Eberwine and Sano. The Official Action refers to Applicants' previous response distinguishing the claimed invention from Eberwine and Sano by pointing out that Eberwine fails to disclose the use of fluorescence in the quantification and that Sano fails to disclose quantification. The Official Action states (for the first time) that the claim does not contain a quantification step.

Applicants have amended claim 1 to clearly set forth the quantification step that refers to measuring quanta of fluorescence signals emitted proportionally to the amount of epitopes present. This amendment clearly renders the claim distinguishable over Eberwine and Sano.

Applicants respectfully request that the rejection of claim 1 under 35 USC §103 in view of Eberwine and Sano be withdrawn.

Claims 15 and 18-20 rejected in view of Eberwine and Sano

Claims 15 and 18-20 are rejected under 35 USC §103 in view of Eberwine and Sano. The Official Action refers to sections in Eberwine that disclose additional limitations set forth in the dependent claims.

As discussed above, claim 1 as amended is distinguished from the combination of Eberwine and Sano. Similarly, claims 15 and 18-20 are distinguished from and patentable over the combination of Eberwine and Sano.

Applicants respectfully request that the rejection of claims 15 and 18-20 under 35 USC §103 in view of Eberwine and Sano be withdrawn.

Claims 11 and 14 rejected in view of Eberwine and Zeytingoglu

Claims 11 and 14 are rejected under 35 USC §103 in view of Eberwine and Zeytingoglu. It is asserted that Eberwine teaches steps a and b of the claimed invention and that Zeytingoglu discloses other amplification techniques such as PCR.

Eberwine neither teaches nor suggests detection of epitopes using RNA amplification in combination with reverse transcriptase or replicase reactions and fluorescence.

Zeytingoglu refers to immunodetection methods and optionally provides for amplification including "two steps, three steps, PAP and APAAP." There is no disclosure anywhere in Zeytingoglu of doing RNA amplification in combination with reverse transcriptase or replicase reactions. The disclosure describes only single PCR amplification. The combination of Eberwine and Zeytingoglu do not yield the present invention. Nowhere is there the teaching or suggestion of RNA amplification in combination with reverse transcriptase or replicase reactions. Zeytingoglu does not address the deficiency of Eberwine. There is no motivation to combine the references and the combination of teachings in the cited references does not yield the instant invention.

Both Eberwine and Zeytingoglu each refer to a single type of oligonucleotide amplification: Eberwine refers to RNA amplification; Zeytingoglu refers to PCR amplification. Eberwine discloses immuno-RNA to detect the presence of antigens. A preferred embodiments disclosed in Eberwine suggests performing the method in a patch pipette. Not only does Eberwine not suggest combining the disclosed immuno-RNA method with a second type of amplification but the preferred embodiment of Eberwine would be difficult if not impossible to adapt to further PCR amplification. Eberwine contains neither a suggestion nor motivation to add an additional type of amplification.

As pointed out in the Official Action, Zeytingoglu discloses that PCR amplification is useful in cases where small amounts of antigen are to be detected. It contains no disclosure or suggestion of further processing PCR amplification products to further increase sensitivity.

In comparing the prior art to the claimed invention, neither reference refers to two type of amplification as distinguished from the claimed invention which does. It is required and implicit in the rejection that either Eberwine or Zeytingoglu must teach or suggest doing a second type of amplification step on the first amplification product yet neither reference provides any disclosure of any further processing beyond the initial type amplification. There is no teaching or suggestion to combine any further amplification techniques and specifically not the two single types of amplification disclosed in the respective references.

The combination of Eberwine and Zeytingoglu do not render the subject matter of claims 11 and 14 prima facie obvious. Not only is there a lack of motivation to combine the references but the combination of references does not yield the present invention. The references teach different types of immuno-amplification technology. In both cases, oligonucleotides attached to antibodies serve as templates for amplification techniques. The combination, which is improper, does not yield the claimed methods because the combination does not yield the use of an amplification product of one reaction serving as the template of a second type of reaction.

Applicants respectfully request that the rejection of claims 11 and 14 under 35 USC §103 in view of Eberwine and Sano as applied to claims 11 and 14 be withdrawn.

Claims 24-26 rejected in view of Eberwine and Zeytingoglu

Claims 24-26 are rejected under 35 USC §103 in view of Eberwine and Zeytingoglu. The Official Action refers to sections in Eberwine that disclose additional limitations set forth in the dependent claims.

As discussed above, claims 11 and 14 are not obvious is in view of the combination of Eberwine and Zeytingoglu. There is no motivation to combine the references and the combination does not yield the claimed invention. Similarly, the combination of Eberwine and Zeytingoglu do not teach or suggest the subject matter of claims 24-26.

Applicants respectfully request that the rejection of claims 24-26 under 35 USC §103 in view of Eberwine and Zeytingoglu be withdrawn.

Claims 21 and 27 rejected in view of Eberwine and Shannon

Claims 21 and 27 are rejected under 35 USC §103 in view of Eberwine as applied to claims 1 and 11, respectively and further in view of Shannon.

Shannon discloses the use of cyanine dyes in linear amplification.

With respect to claim 21, it is dependent on claim 1, which has been amended. As discussed above, claim 1 has been amended to clearly distinguish the subject matter in the claim from that disclosed in the combination of Eberwine and Sano. As amended, claim 1, from which claim 21 depends, is patentable over Eberwine. While Shannon discloses the use of cyanine dye to stain antisense RNA produced by RNA amplification of a cDNA generated from mRNA, it does not compensate for the shortcomings of the prior art with respect to amended claim 1. Accordingly, the combination of Eberwine and Shannon do not render the subject matter of claim 21 obvious.

With respect to claim 27, it is dependent on claim 11. As discussed above, claim 11 is patentable over the combination of Eberwine and Zeytingoglu. There is no motivation to combine the references and the combination does not yield the claimed invention. The combination of Eberwine and Zeytingoglu do not teach or suggest the subject matter of claim 11. While Shannon discloses the use of cyanine dye to stain antisense RNA produced by RNA amplification of a cDNA generated from mRNA, it does not compensate for the shortcomings of the prior art with respect to claim 11. Accordingly, the combination of Eberwine and Shannon do not render the subject matter of claim 27 obvious.

Applicants respectfully request that the rejection of claims 21 and 27 under 35 USC §103 in view of Eberwine and Shannon be withdrawn.

Allowable Subject Matter

Objections to Claims 16, 17, 22 and 23

Claims 16, 17, 22 and 23 have been objected to as being dependent on a rejected base claim. The Official Action states that the claims would be allowable if rewritten in independent form including the base claims and all intervening claims.

Claims 16 and 22 have been amended to be placed in independent form including all of the limitations found in the base claims from which the claims previously depended (claims 1 and 11,

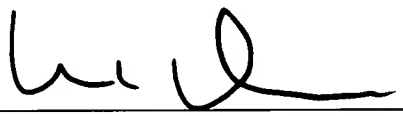
respectively). Claims 17 and 23 are dependent on claims 16 and 22, respectively, and thus contain all of the limitations of amended claims 16 and 22.

As amended, claims 16, 17, 22 and 23 are in allowable form.

Conclusion

Applicants respectfully urge that claims 1, 11, and 14-27 be allowed at this time.

Respectfully submitted,



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